PHYSIOLOGY OF THE RESPIRATORY SYSTEM

No. 522

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A.

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TOBACCO INDUSTRY RESEARCH COMMITTEE
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COMMITTEE:
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Application For Research Grant

Date: December 23, 1965

1. Name of Investigator: Richard O. Bicks, M.D., FACP; E. William Rosenberg, M.D., FACP, Miguel A. Azar, M.D., Ph.D.

2. Title: Dr. Bicks: Assistant Professor, Department of Medicine
Dr. Rosenberg: Assistant Professor, Division of Dermatology
Dr. Azar: Research Fellow in Immunology

3. Institution & Address: University of Tennessee College of Medicine
62 South Dunlap
Memphis, Tennessee 38103

4. Project or Subject: Experimental Delayed Hypersensitivity Reactions of the Respiratory System.

5. Detailed Plan of Procedure (Use additional pages if more space is required.)

We have previously reported on the production of a chronic delayed hypersensitivity reaction in the gastrointestinal tract. With the use of a low molecular weight chemical 2-4 D:nitro-chlorobenzene and an inert vehicle, Orabase, mucosal allergy of the contact type was localized in the colon and small intestine. The histological lesion in the colon showed mucosal ulceration with hemorrhage infiltration of the lamina propria with lymphocytes, perivascular cuffing, vascular engorgement and giant cell systems in the submucosa. This lesion is independent of the concentration of the contactant; depends on the frequency of application of the contactant and can be partially modified by immunosuppressive drugs. These lesions are immunologically specific and primary contact sensitization has been achieved, i.e., the lesion has been produced without prior skin sensitization. This work has been called the best experimental model of human ulcerative colitis to date. References to this work are cited below.

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We are currently investigating the specific nature of this immunological reaction, its localization on other parts of the gastrointestinal tract, and the relationship of gastric mucosal damage to parietal cell antibodies.

In the course of these studies, we made preliminary observations of this reaction localized in the respiratory tract. In four animals we produced a chronic pneumonitis and bronchitis. We propose to extend these observations in a systematic manner.

Pigs were chosen as the experimental animal because they react identically to man in terms of contact sensitivity. We plan to use 25 dewormed miniature pigs obtained from the Hormel Institute. They will be divided into five groups of animals. All animals will have a tracheostomy. Control group I will have this only. Control group II will be skin sensitized to a 2% solution of DNCB. Control group III will have Oradhesive powder blown into their tracheobronchial tree by IPPB. Experimental groups IV and V will be skin sensitized to DNCB and have plain DNCB and DNCB in Oradhesive instilled in their tracheobronchial trees. Each animal will be treated daily and sacrificed at intervals and examined morphologically. When a consistent histological lesion is produced the experiment will be repeated to establish a chronic lesion, and treatment response to antibiotics, immunosuppressive drugs and steroids studied. We hope to identify a chronic delayed hypersensitivity reaction in the respiratory tree.

Salaries are for the director, Dr. Bicks; two research associates, Dr. Rosenberg and Dr. Azar, one full time research technician and two part time animal caretakers. Expendable supplies include animal costs, care and feeding of animals and chemicals needed.

Dr. Bicks is a Diplomate, American Board of Internal Medicine and its Sub-Specialty Board on Gastroenterology. He is a member of the American Gastroenterological Association and a Fellow of the American College of Physicians.

Dr. Rosenberg is a Diplomate of the American Board of Dermatology and a Fellow of the American College of Physicians. He is a consultant to the U. S. Naval and Veterans Administration Hospitals.

Dr. Azar is an M.D. with graduate training in Pediatrics and a Ph.D. in Immunology.

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Source: https://www.industrydocuments.ucsf.edu/docs/tvwm0000

Pertinent references include:

1. Rosenberg, E. W., and Fischer, R. W., Improved Method for Intraoral Patch Testing, Arch. Derm. 87:115, 1963.

2. Rosenberg, E. W., and Fischer, R. W., DNCB Allergy in the Guinea Pig Colon, Arch. Derm. 89:99, 1964.

3. Bicks, R. O., and Rosenberg, E. W., A Chronic Delayed Hypersensitivity Reaction in the Guinea Pig Colon, Gastroenterology 46:543, 1964.

4. Bicks, R. O., Rosenberg, E. W., et al, Further Observations on a Delayed Hypersensitivity Reaction in the Guinea Pig Colon, Gastroenterology, 48:425, 1965.

5. Bicks, R. O., Rosenberg, E. W., et al, Primary Induction of a Contact Hypersensitivity Reaction in the Swine Colon, Gastroenterology, (In Press).

6. Bicks, R. O., Rosenberg, E. W. and Azar, M., A Contact Hypersensitivity Reaction in the Small Bowel of Swine Associated with Xylose Malabsorption, (In Preparation).

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Source: https://www.industrydocuments.ucsf.edu/docs/[illegible]

6. Budget Plan:

a.	Salaries	$ 60,000.00
b.	Expendable Supplies	5,000.00
c.	Other Expenses	3,000.00
d.	Permanent Equipment	3,000.00
e.	Overhead (15% of a, b, c)	10,200.00
	Total	81,200.00

7. Anticipated Duration of Work: 2 years @40,600 each

8. Facilities and Staff Available: All facilities of the Medical-Surgical Research Laboratories of the Kennedy Veterans Hospital, Memphis, Tennessee, and the University of Tennessee College of Medicine, Memphis, Tennessee, are available to us.

9. Additional Requirements: None

10. Additional Information (Including relation of work to other projects and other sources of support):

The work on the gastrointestinal tract is supported by Grant #09384 of the NIH, General Medicine Section of the National Institute of Arthritis and Metabolic Diseases. This will expire in December, 1968. We have established techniques, quarters, and skilled animal handlers. This supplemental grant will enable us to extend our observations to another system using procedures we have developed.

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Signature Richard Q. Bicks, M.D.

Director of Project

Homer F. Marsh

Business Officer of the Institution

Homer F. Marsh, Ph.D., Vice President

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